=> s 112

L13 16 L12

=> d abs fbib hitstr 1-16

L13 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

- AB The title compds. I [one of XI-X3 = S, and the other two represent C or N atoms; ring A = 6-10 membered aryl, 5-13 membered heteroaryl or partially aromatic heterocyclyl; R1 = H, halo, OH, CO2H, etc.; R2, R3 = H, alkyl, haloalkyl, etc.; n = 2-4; R4 = H, halo, S(alkyl), CN, etc.], that are useful for treating atherosclerosis, dyslipidemias and the like, were prepared and disclosed. E.g., a multi-step synthesis of II, starting from 3-(2-naphthyl)acrylic acid, was given. Compds. I generally have an IC50 in the 3H-nicotinic acid competition binding assay within the range of 1 nM to about 25 μM. Also compds. I generally have an EC50 in the functional in vitro GTPγS binding assay within the range of about less than 1 μM to as high as about 100 μM. Pharmaceutical compns. comprising the compound I alone or in combination with DF receptor antagonist, are also included.
- AN 2007:1204726 CAPLUS Full-text
- DN 147:486319
- TI Preparation of N-(2-carboxythienyl) amides as niacin receptor agonists
- IN Colletti, Steven L.; Tata, James R.; Chen, Weichun; Beresis, Richard T.; Ding, Fa-Xiang; Schmidt, Darby Rye; Shen, Hong; Raghavan, Subharekha
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 58pp.
  - CODEN: PIXXD2
    T Patent
- DT Patent LA English
- LA English

FAN.CNI I																				
		PAT	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D	ATE		
								-												
	PI	PI WO 2007120575					A2 20071025			WO 2007-US8584						20070406				
			W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	CA,	
				CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	
				GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	
				KN,	KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	ME,	MG,	
				MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	ΝI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	
				RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,	TN,	TR,	
				TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	zw						

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GM, GQ, GW, MI, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006-791019P P 20060411

OS MARPAT 147:486319

TT 668356-71-0 688356-89-0 668356-90-3 668356-90-3 668356-95-8 688357-06-4 668357-08-6 688357-09-7 688357-11-1 688357-12-2 688357-13-3 688357-14-4 688357-15-5 794558-37-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (co-drug; preparation of N-(2-carboxythienyl) amides as niacin receptor agonists)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 794535-37-8 CAPLUS
- CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

GI

- \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT \*
- AB Title compds. I [X = C or N; Z = (un)substituted aryl or heteroaryl; Rl independently = H, halo, COZH, CN, etc.; R2 and R3 independently = H, alkyl, haloalkyl, alkoxy, etc.; R4 = H, F, or (un)substituted alkyl; R5 = COZH, tetrazole, or CONHSOZR6 wherein R6 = (un)substituted alkyl or phenyl; m and p = 1 or 2 such that their sum = 3; n = 2-4; A = 6-10 membered ], as well as their pharmaceutically acceptable salts are prepared and disclosed as useful for treating atherosclerosis, dyslipidemias and the like. Thus, e.g., II was prepared by conversion of 3-(4- bromophenyl)propionic acid to the amide with N-hydroxysucchimide followed by reaction with triflate III to form the 4-bromophenylpropionamide derivative which was coupled with 4-hydroxyphenylboronic acid and hydrolyzed to give the desired product. In the 3H-nicotinic acid competition binding assay, I demonstrated IC50 values ranging from 1 nM to about 25 µM. Pharmaceutical compns. and methods of use are also included.
- AN 2007:912171 CAPLUS Full-text
- DN 147:277179
- TI Preparation of carboxamidocyclohexenylcarboxylic acids derivatives as niacin receptor agonists, compositions containing such compounds and methods of treatment
- IN Raghavan, Subharekha; Schmidt, Darby Rye; Colletti, Steven L.; Smenton, Abigail Lee
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 96pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	WO 2007092364	A2	20070816	WO 2007-US2994	20070202
	W: AE, AG, AL,	AM, AT,	AU, AZ, BA,	BB, BG, BR, BW, BY,	BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, JT, TM, TN, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BE, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006-765853P P 20060207

OS MARPAT 147:277179

OS MARKAI 19:7/17/9

IT 698356-71-0 688356-89-0 698356-90-3 688356-95-8 688357-06-4 688357-08-6 688357-09-7 688357-10-0 698357-11-1 688357-12-2 688357-13-3 688357-14-4 688357-15-5 794535-37-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(claimed co-drugs for administration; preparation of cyclohexylcarboxylates as niacin receptor agonists)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688356-89-0 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylthio)- (CA INDEX NAME)

- RN 688356-90-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688356-95-8 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromopheny1)thio]-6,7,8,9tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

- RN 688357-06-4 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-08-6 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4-methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-CN 6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GΙ

- AB Title compds. [I; Q = (R1)3A[C(Ra)2]xCRb(NR2R3)(CHRc)y; A = aryl, heteroaryl; B = atoms to form Ph, thienyl, cyclohexenyl ring; R1 = H, halo, OH, CO2H, cyano, NH2, CORe, aminoalkyl, CONH2, (substituted) Ph, heteroaryl, etc.; Re = (substituted) alkyl, Ph; Ra, Rb, RC = H, alkyl, haloalkyl; R2, R3 = H, alkyl, haloalkyl; R4 = H, halo, (substituted) alkyl, aryl, heteroaryl, heterocyclyl, etc.; 1 of x, y = 0, the other = 1], were prepared Thus, N-(tertbutoxycarbonyl)-3-(2-naphthyl)-L-alanine in CH2Cl2 at -10° was treated with DCC, HOBT, and Et 2-aminobenzoate followed by stirring for 12-24 h to give a residue which was treated with KOH in THF/MeOH/H2O and then with CF3CO2H in CH2Cl2 to give title compound (II). I in the functional in vitro GTPYS binding assay showed EC50 values of about 1-100 µM.
- AN 2007:728973 CAPLUS Full-text
- DN
- Preparation of (hetero)arvl amino acid amides as niacin receptor agonists for treatment of atherosclerosis, dyslipidemia, diabetes, and metabolic syndrome.
- Imbriglio, Jason; Colletti, Steven L.; Tata, James R.; Beresis, Richard T.; Marley, Daria; Raghavan, Subharekha; Schmidt, Darby Rye; Lins, Ashley Rouse; Smenton, Abigail L.; Chen, Weichun; Shen, Hong; Ding, Fa-Xiang; Bodner, Rena
- Merck & Co., Inc., USA PA
- SO PCT Int. Appl., 78pp.
  - CODEN: PIXXD2 Pat.ent.
- English LA

FAN.CNT 1

	PATENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE			
						-													
PI	WO 2007	0757	49		A2		20070705		WO 2006-US48535						20061220				
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		GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,		
		KP,	KR,	KZ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,		
		MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,		
		RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM,	TN,	TR,	TT,		
		TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW								
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		IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,		
		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,	GH,		
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,		
		KG,	KZ,	MD,	RU,	TJ,	TM												
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IT 688356-71-0 688356-89-0 688356-90-3 688356-95-8 688357-06-4 688357-08-6 688357-09-7 688357-10-0 688357-11-1 688357-12-2 688357-13-3 688357-14-4 688357-15-5 794535-37-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of (hetero)aryl amino acid amides as niacin receptor agonists for treatment of atherosclerosis, dyslipidemia,

diabetes, and metabolic syndrome)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

688356-89-0 CAPLUS CN

Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4-methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

- Title compds. [I; 1-3 of W, X, Z = heteroatoms, the other = C; Y = C, N; 0-1 AB of W, X, Z = O, S, the remainder of W, X, Z = C, N; ring containing W, X, Y, Z is aromatic; A = 9-10 membered aryl, 8-10 membered heteroaryl, partially aromatic heterocyclyl; R1 = H, OH, halo, cyano, (substituted) alkyl, alkenyl, alkynyl, etc.; R2 = H, (substituted) alkyl, alkenyl; R3 = H, halo, Me, halomethyl; dotted lines = optional double bonds, either both present or both absent], were prepared Thus, title compound (II) was prepared from 4-bromo-3methylthiophene-2-carboxylic acid, 6-hydroxy-2-naphthylboronic acid, and anthranilic acid. In a 3H-nicotinic acid competition binding assay, I showed IC50's of about 10 nM-25 uM.
- AN 2007:351935 CAPLUS Full-text
- DN 146:379811
- ΤI Preparation of heterocyclylcarbonylaminobenzoic acids as niacin receptor agonists
- TN Colletti, Steven L.; Imbriglio, Jason E.; Beresis, Richard Thomas; Frie, Jessica Leslie
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 54pp.
- CODEN: PIXXD2
- DT Patent LA English

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	PATENT NO.					KIND DATE				APPLICATION NO.					DATE				
PI								0329 1122		WO 2	006-	US36	023		2	0060	915		
	W: RW:	CN, GE, KR, MW, RU, UA, AT, IS, CF,	CO, GH, KZ, MX, SC, UG, BE, IT, CG, KE,	CR, GM, LA, MY, SD, US, BG, LT, CI, LS,	CU, HN, LC, MZ, SE, UZ, CH, LU, CM, MW,	CZ, HR, LK, NA, SG, VC, CY, LV, GA, MZ,	DE, HU, LR, NG, SK, VN, CZ, MC, GN, NA,	AZ, DK, ID, LS, NI, SL, ZA, DE, NL, GQ, SD, AP,	DM, IL, LT, NO, SM, ZM, DK, PL, GW, SL,	DZ, IN, LU, NZ, SV, ZW EE, PT, ML, SZ,	EC, IS, LV, OM, SY, ES, RO, MR, TZ,	EE, JP, LY, PG, TJ, FI, SE, NE,	EG, KE, MA, PH, TM, FR, SI,	ES, KG, MD, PL, TN, GB, SK, TD,	FI, KM, MG, PT, TR, GR, TR,	GB, KN, MK, RO, TT, HU, BF, BW,	GD, KP, MN, RS, TZ, IE, BJ, GH,		
	AU 2006	2925	59		A1		2007	0329		AU 2 US 2	005- 006- 005-	2925 7186	59 22P	1	2 P 2	0050 0060 0050	915 920		
OS IT	MARPAT 688356- 688356- 688357-	71-0 95-8 09-7	688 688 688	356- 357- 357-	06-4 10-0	588 688	357- 357-	08-6 11-1		2	0				<b>.</b>				

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688357-12-2 688357-13-3 688357-14-4
688357-15-5 794535-37-8
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration; preparation of heterocyclylcarbonylaminobenzoic acids as niacin receptor agonists)

RN 688356-71-0 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-CN tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-11-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

- RN 688357-12-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-13-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

Title compds. I [wherein X = C or N; D = bond, O, CH2, CH2CH2 or CH2CH2CH2; B AB = (hetero)aryl; B' = H or absent; B and B' can be taken together to form a spiro ring while D = bond; Ra = H, halo, OH, etc.; Rb = H, halo, alkyl, etc.; Rc = COOH or tetrazol-5-vl; R4 = H, halo or (halo)methyl, with limitations or pharmaceutically acceptable salts and solvates were prepared as niacin receptor agonists. Solid-phase synthesis of I such as II on Wang resin was disclosed. The invented compds, generally have EC50 in the range of 1 µM to 100  $\mu\text{M}$  for niacin receptor in the binding assay. I are useful for the treatment of atherosclerosis, dyslipidemia, diabetes and other conditions.

AN 2007:259556 CAPLUS Full-text

146:316951 DN

ΤI Preparation of piperazinecarboxamides, diazepanecarboxamides and their analogs as niacin receptor agonists for the treatment of atherosclerosis. dyslipidemia and diabetes

Colletti, Steven L.; Shen, Hong; Tata, James R.; Szymonifka, Michael J. IN

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 55pp.

CODEN: PIXXD2

DT Patent

LA English

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ΡI	WO 2007027532																	
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			CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,
			GM,	KE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
			KG,	ΚZ,	MD,	RU,	ТJ,	TM										
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											US 2	005-	7122	75P	1	P 2	0050	829
											WO 2	006-	US33	304	1	n 2	0060	825
	CA	2620	570			A1		2007	0308		CA 2	006-	2620	570		2	0060	825
											US 2	005-	7122	75P	1	P 2	0050	829
											WO 2	006-	US33	304	1	n 2	0060	825

OS MARPAT 146:316951

II 688356-71-0 688356-89-0 688256-90-3 688356-90-3 688357-06-4 688357-08-6 688357-09-7 668357-10-0 688357-12-3 688357-12-3 688357-13-3 688357-14-4 683357-15-5 794535-37-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (co-drug; preparation of piperazinecarboxamides, diazepanecarboxamides and their analogs as niacin receptor agonists for treatment of atherosclerosis, dyslipidemia and diabetes)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-10-0 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-11-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-12-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4-methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

Title compds. I [X = CH2, O, S, etc.; a, b = 1-3 such as a + b = 2-4; ring A = AB aryl, heteroaryl, partially aromatic heterocyclic group, said heteroaryl and partially aromatic heterocyclic group containing at least one heteroatom selected from O, S, SO, etc., and optionally containing 1 other heteroatom selected from O and S, and optionally containing 1-3 addnl. N atoms, with up to 5 heteroatoms being present; R2, R3 = H, alkyl, haloalkyl, etc.; n = 1-5; R4 = H, halo, R6; R6 = alkyl optionally substituted with 1-3 groups, 0-3 of which are halo, and 0-1 of which are selected from the group consisting of 0alkyl, hydroxy, amino, etc.; R5 = -CO2H, tetrazol-5-yl, etc.; R1 = H, halo, hydroxy, etc.], pharmaceutically acceptable salts or solvates thereof were prepared For example, reaction of 3-(naphthalen-2-v1)propionic acid with methanesulfonyl chloride followed by in-situ treatment with Me 2aminocyclohex-2-ene-1-carboxylate and hydrolysis using NaOH afforded compound II. The invented compds. generally have an IC50 in the 3H-nicotinic acid competition binding assays within the range of 1 nM to about 25 µM, and have an EC50 in the functional in vitro GTPVS binding assays within the range of about 1-100 μM.

- AN 2006:1356948 CAPLUS Full-text
- DN 146:100362
- TI Preparation of 2-acylaminocycloalkenecarboxylic acids derivatives as niacin receptor agonists
- IN Raghavan, Subharekha; Colletti, Steven L.; Ding, Fa-Xiang; Shen, Hong; Tata, James R.; Lins, Ashley Rouse; Smenton, Abigail Lee; Chen, Weichun; Schmidt, Darby Rye; Tria, George Scott
- PA USA
- SO U.S. Pat. Appl. Publ., 69pp.
- CODEN: USXXCO
- DT Patent
- LA English

PATENT NO.						KIND		DATE				LICAT					ATE	
PI		2006				A1		2006			US	2006-	4746	46		2	0060	626
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	AU	2006	2618	39		A1		2007	0104			2006-					0060	
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	CA	2611	552			A1		2007	0104			2006-					0060	
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	KR	2008	0196	53		A		2008	0304			2007-					0071	
											US	2005-	694/				0050 0060	

## OS MARPAT 146:100362

- IT 688356-71-0 688356-89-0 688356-90-3 688356-95-8 688357-06-4 688357-08-6
  - 688357-09-7 688357-10-0 688357-11-1 688357-12-2 688357-13-3 668357-14-4
  - 688357-12-2 688357-13-3 668357-14
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    (medicaments with; preparation of 2-acylaminocycloalkenecarboxylic acids as
    niacin receptor agonists)
- RN 688356-71-0 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-11-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-12-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-13-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

- AB Title compde. represented by the formula I [wherein Rl = (un)substituted cyclohexyl, Ph or heteroaryl, R2 = tetrazol-5-yl, 2,4-dioxo-oxazol-5-yl or CO2R; R = H or alkyl; n = 1 or 2; and pharmaceutically acceptable salts or solvates thereof] were prepared as Niacin receptor agonists. For example, II was provided in a multi-step synthesis starting from 3-ethoxy cyclopentenone. Certain I an ICSO in the niacin binding assay within the range of about 0.010-50 µM, and have an ECSO in the functional GTPS binding assay within the range of about 0.010-100 lM. Thus, I and their pharmaceutical compons. are useful as Niacin receptor agonists for the treatment of dyslipidemias (no data).
- AN 2006:1124674 CAPLUS Full-text
- DN 145:455008
- TI Preparation of pyrazole derivatives as Niacin receptor agonists
- IN Imbriglio, Jason E.; Colletti, Steven L.; Tata, James R.; Liang, Rui; Raghavan, Subharekha; Schmidt, Darby R.; Smenton, Abigail R.; Chan, Sook Yee
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 83pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

E MIN.							KIND DATE				APPLICATION NO.									
PI	WO 2006113150					2006									0060	407				
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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,	KΡ,	KR,			
		KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	MX,			
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		VN,	YU,	ZA,	ZM,	ZW														
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		IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,			
		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,	GH,			
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	AU 20	062369	39		A1		2006	1026		AU 2						0060				
										US 2										
										WO 2						0060				
	CA 26	03757			A1		2006	1026		CA 2						0060				
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										US 2										
										WO 2	006-	US12	876		W 2	0060	407			

IN 2007CN04216	A	20071221	IN 2007-CN4216		20070924
			US 2005-670764P	P	20050413
			WO 2006-US12876	W	20060407
CN 101160125	A	20080409	CN 2006-8001206	õ	20071012
			US 2005-670764P	P	20050413

WO 2006-US12876 W 20060407

OS MARPAT 145:455008

68356-71-0P 688356-89-0P 688356-90-3P 688356-95-8P 688357-08-6P 688357-08-6P 688357-08-6P 688357-10-0P 688357-11-1P 688357-12-2P 688357-13-3P 688357-14-4P 688357-15-5P 794535-37-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazole derivs. as Niacin receptor agonists)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

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- AB A method of treating atherosclerosis is disclosed wherein nicotinic acid or another nicotinic acid receptor agonist is administered to the patient in combination with a DP (prostaglandin D2) receptor antagonist. E.g, I was prepared by a series of reactions starting from 4-chloronicotinaldehyde. The compds, prepared function as selective DP antagonists and demonstrate an affinity for DP that is at least about 10 times higher than the affinity for CRTH2 receptors.
- AN 2006:844718 CAPLUS Full-text
- DN 145:271745
- TI Preparation of pyridoindolizine and pyridoindole derivatives for treating atherosclerosis, dyslipidemias and related conditions
- IN Fitzpatrick, Shaun; Seiler, Christian; Hardy, Ian; Waters, M., Gerard; Lai, Eseng
- PA Merck & Co., Inc., USA
  - O PCT Int. Appl., 66pp.
- CODEN: PIXXE
- DT Patent
- LA English

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688356-71-0P 688356-89-0P 688356-90-3P											WO	2006-1	JS69	51	1	W 2	0060	215		
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688356-95-8P 688357-06-4P 689357-08-6P 688357-09-7P 688357-10-0P 689357-11-1P 689357-12-2P 688357-13-3P 688357-14-4P 689357-15-5P 794535-37-8P 887146-39-6P 87146-49-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridoindolizine and pyridoindole derivs for treating atherosclerosis, dyslipidemias and related conditions)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-11-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

- RN 688357-12-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-13-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

RN 887146-39-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (6S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 887146-40-9 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (6R)- (CA INDEX NAME)

Absolute stereochemistry.

IT 688356-87-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridoindolizine and pyridoindole derivs for treating atherosclerosis, dyslipidemias and related conditions)

RN 688356-87-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, ethyl ester (CA INDEX NAME)

AR The invention relates to certain fused pyrazole derivs. of formula I, and pharmaceutically acceptable salts thereof, which exhibit useful pharmacol. properties, for example, as agonists for the RUP25 receptor. Compds. of formula I wherein X is N, and Z is CR7, or X is CR7 and Z is N; one dotted lines are single and double bonds such that the ring containing X and Z is a pyrazole ring; R1 - R6 are independently H, C1-6 acyl(oxy), C2-6 alkenyl, C1-6 alkoxy, C1-6 alkyl(amino), C1-6 alkyl(thio)carboxamide, C2-6 alkynyl, etc.; R7 is carbo-C1-6 alkoxy, carboxy, or tetrazol-5-yl; and their pharmaceutically acceptable salts, hydrates, or solvates thereof are claimed. Also provided by the invention are pharmaceutical compns. containing compds. of the invention, and methods of using the compds, and compns, of the invention in the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like. In addition, the invention also provides for the use of the compds. of the invention in combination with other active agents such as those belonging to the class of  $\alpha$ -glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme (ACE) inhibitors, insulin secretion enhancers, DP receptor antagonists, and the like. Example compound II was prepared by cyclization of (R)-2-(3butenvl)oxirane; the resulting bicvclo[3.2.1]hexan-2-ol underwent oxidation of give bicyclo[3.2.1]hexane-2-one, which underwent cyclization with di-Et oxalate and hydrazine to give 1a, 2, 5, 5a-tetrahydro-1H-2, 3diazacyclopropa[a]pentalene-4-carboxylic acid Et ester, which underwent amidation with ammonium hydroxide to give the corresponding amide, which benzylation with benzyl bromide followed by dehydration to give 2-benzyl-1a, 2, 5, 5a-tetrahydro-1H-2, 3-diazacyclopropa[a]pentalene-4- carbonitrile, which reacted with sodium azide to give 2-Benzyl-4-(2H- tetrazol-5-yl)-la,2,5,5atetrahydro-2,3-diazacyclopropa[a]pentalene, which underwent debenzylation to give example compound II. All the invention compds. were evaluated for their antihyperglycemic activity, and 35S-GTPyS, human RUP25, and 3H-nicotinic acid receptor binding affinities. Certain compds. were determined to have an EC50 value in the cAMP whole cell method of about 25 uM or less. From the in vitro GTPyS binding assay, it was determined that tested compds. exhibited EC50 values in the range of about 1-100 μM, and the best compds. showed an EC50 value of less than about 1 uM. Certain tested compds. have an EC50 in the 3Hnicotinic acid binding competition assay, in the range of 1 to  $100~\mu\mathrm{M}$  , and the most favorable compds. exhibited an EC50 value of less than about  $1\ \mathrm{uM}.$ 2006:635044 CAPLUS Full-text AN

DN 145:103670

TI Fused pyrazole derivatives and their preparation, pharmaceutical compositions, and methods for treatment of metabolic-related disorders IN Boatman, Douglas P.; Schrader, Thomas O.; Semple, Graeme; Skinner, Philip

J.; Jung, Jae-Kyu

PA Arena Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DT Patent

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P 20041223 US 2004-638668P US 2005-676521P P 20050429 WO 2005-US46599 W 20051222

OS MARPAT 145:103670

688356-71-0P 688356-89-0P 688356-90-3P ΙT 688356-95-8P 688357-06-4P 688357-08-6P 688357-09-7P 688357-10-0P 688357-11-1P 688357-12-2P 688357-13-3P 688357-14-4P 688357-15-5P 794535-37-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of fused pyrazole derivs. and methods for treatment of metabolic-related disorders)

688356-71-0 CAPLUS RN

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)



RN 688356-89-0 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-CN tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

AB The invention is related to biaryls I [Y = C, N; Z = C(RaRb)n; Ra, Rb = independently H, alkyl, OH, F, etc.; n = 1-5; Rl = CO2H, lH-tetrazol-5-yl, CONHSO2Rc; Rc = (un)substituted alkyl, Ph; XlO! = (X10)0-1; Xl' = (X1)0-1' Xl- XlO = C, or a heteroatom selected from O, S, and N, with provisos; each R2 = H, F, Cl, Br, I, alkyl, heterocyclyl, etc.; or two R2 groups taken together can form a fused Ph or fused heterocycle with ring B; each R3 = H, halo, halo/alkyl, halo/alkoxy, etc.; each R4 = H, halo, Me, etc.], as well as pharmaceutically acceptable salts, solvates, as niacin receptor agonists useful for treating atherosclerosis and dyslipidemias in combination with DP antagonists. The invention is also related to the preparation of DP antagonists. Pharmaceutical compns. comprising I are also included. Thus, anthranilide II was prepared by Pd-coupling of 3-(4-iodophenyl)propionic acid with phenylboronic acid, chlorination of biaryl propionic acid (no data) with

SOC12, and amidation of acyl chloride (no data) with anthranilic acid. I have an EC50 in the functional assay in vitro GTPyS binding assay within the range of about less than 1  $\mu M$  to as high as about 100  $\mu M$ . Have an IC50 in the 3H-nicotinic acid competition binding assay within the range of 1 nM to about 25  $\mu M$ . Selected I do not exhibit measurable in vivo vasodilation in the murine flushing model at doses up to 100 mg/kg or 300 mg/kg in the presence of DP antagonists.

AN 2006:513667 CAPLUS Full-text

DN 145:27731

TI Preparation of biaryl compounds, particularly N-

(biarylpropionyl)anthranilides, as niacin receptor agonists and pyridoindolizine derivatives as DP receptor antagonists, their pharmaceutical compositions and their combination useful for treating atherosclerosis and dyslipidemias

IN Colletti, Steven L.; Tata, James R.; Shen, Hong C.; Ding, Fa-Xiang; Frie, Jessica L.; Imbriglio, Jason E.; Chen, Weichun

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DT Patent LA English

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OS MARPAT 145:27731

IT \$88356-71-0P, [5-[(4-Chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9tetrahydropyrido[3,2-b]indolizin-6-yl]a cetic acid 688356-89-0F, [5-[(4-Chlorophenyl)sulfanyl]-4-(methylthio)-6,7,8,9-tetrahydropyrido[3,2b]indolizin-6-yl]acetic acid 688356-99-3P, [5-[(3,4-Dichlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[3,2blindolizin-6-vllacetic acid 688356-95-8P, [5-[(4-Bromophenyl)thio|-4-(methylsulfonyl)-6,7,8,9-tetrahydropyrido|3,2blindolizin-6-vllacetic acid 688357-06-4P, [10-[(3.4-Dichlorophenvl)sulfanvl]-1-(methylsulfonvl)-6,7,8,9-tetrahydropyrido[3,4b]indolizin-9-yl]acetic acid 688357-08-6P, [4-(Methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]-6,7,8,9-tetrahydropyrido[3,2-b]indolizin-6-yl]acetic acid 688357-09-7P, [5-[(2-Chloro-4fluorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[3,2b]indolizin-6-yl]acetic acid 688357-10-0P 688357-11-1P 688357-12-2F, [5-[(4-Methylphenyl)thio]-4-(methylsulfonyl)-6,7,8,9tetrahydropyrido[3,2-b]indolizin-6-yl]acetic acid 638357-13-3P, [4-(Methylsulfonyl)-5-(phenylthio)-6,7,8,9-tetrahydropyrido[3,2blindolizin-6-vllacetic acid 688357-14-4P 688357-15-5P , [5-[(4-Chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9tetrahydropyrido[4,3-b]indolizin-6-yl]acetic acid RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(DP receptor antagonist; preparation of biaryl compds. as niacin receptor agonists and pyridoindolizine derivs. as DP receptor antagonists and their combination useful for treating atherosclerosis and dvelinidemias)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromopheny1)thio]-6,7,8,9tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4-methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

L13 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

- AB A method of treating pathol, blushing is disclosed wherein the patient is administered a DP (prostaglandin D2) receptor antagonist. E.g, I was prepared by a series of reactions starting from 4-chloronicotinaldehyde. The compds. prepared function as selective DP antagonists and demonstrate an affinity for DP that is at least about 10 times higher than the affinity for CRTH2 receptors.
- 2006:471897 CAPLUS Full-text AN
- DN 144:488635
- Preparation of compounds such as pyridoindolizine and indole derivatives as prostaglandin D2 antagonists for treating pathological blushing
- - Tobert, Jonathan A.; Lai, Eseng
- PA Merck & Co., Inc., USA PCT Int. Appl., 40 pp. SO
- CODEN: PIXXD2
- Patent
- English LA
- FAN CNT 1

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	WO 2006052798	A2	20060518	WO 2005-US40117	20051107
	WO 2006052798	A3	20070111		
	W: AE, AG, AL,	AM. AT	. AII. AZ. BA.	BB. BG. BR. BW. BY.	BZ. CA. CH.

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM US 2004-625823P P 20041108 US 20070299122 20071227 US 2007-667346 20070508 A1 US 2004-625823P P 20041108

WO 2005-US40117

W 20051107

S CASREACT 144:488635

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68355-71-0P 689356-89-0P 688356-90-9P 668356-95-8P 689357-06-4P 688357-08-6P 688357-09-7P 688357-11-1P 688357-112-2P 688357-13-3P 689357-14-4P 688357-115-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of compds. such as pyridoindolizine and indole derivs. as prostaglandin D2 antagonists for treating pathol. blushing) 688356-710 CAPLUS

RN 688356-71-0 CAPLUS
CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688356-89-0 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4-methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

IT 688356-87-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of compds. such as pyridoindolizine and indole derivs. as prostaglandin D2 antagonists for treating pathol. blushing)

RN 688356-87-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)-, ethyl ester (CA INDEX NAME)

IT 794535-37-8P 887146-39-6P 887146-40-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of compds. such as pyridoindolizine and indole derivs. as prostaglandin D2 antagonists for treating pathol. blushing)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

- RN 887146-39-6 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (6S)- (CA INDEX NAME)

Absolute stereochemistry.

- RN 887146-40-9 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (6R)- (CA INDEX NAME)

Absolute stereochemistry.

$$\mathbf{B} = (\mathbf{CR}^{1}\mathbf{R}^{2})_{n} \qquad \qquad \mathbf{R}^{3} \qquad \qquad \mathbf{R}^{4})_{2}$$

- AR The invention relates to miacin receptor agonists of formula I; as well as pharmaceutically acceptable salts and solvates. The compds. are useful for treating dyslipidemias, and in particular, reducing serum LDL, VLDL and triglycerides, and raising HDL levels. Pharmaceutical compns. and methods of treatment are also included. Compds. of formula I wherein Y is C or N: R1 and R2 are independently H, (halo)C1-3 alkyl(oxy), OC1-3 alkyl, OH, or F; R3 is Co2H, tetrazolyl, or CONHSO2H and derivs.; R4 is H, halo, or (halo)methyl; B is (un)substituted 10-membered bicyclic arvl, (un)substituted 9- to 10membered bicyclic heteroaryl, or (un)substituted 12- to 13-membered tricyclic heteroaryl; n is an integer from 1 to 4, such that when (CR1R2)n represent CH(Me)CH2, the ring B is (un)substituted bicyclic aryl; and their pharmaceutically acceptable salts and solvates thereof. Example compound II was prepared by amidation of 3-(1-naphthyl)acrylic acid with Me anthranilate followed by catalytic hydrogenation. All the invention compds, were tested for their niacin receptor affinity. From the assay, it was determined that most of the compds. in general exhibited in vitro EC50 values in the range of about 1 uM to as high as about 100 uM.
- AN 2006:469551 CAPLUS Full-text
- DN 144:488409
- TI N-Acyl anthranilic acid and related compounds as niacin receptor agonists, and their preparation, pharmaceutical compositions and methods of treatment of dvslipidemias
- IN Colletti, Steven L.; Beresis, Richard T.; Chen, Weichun; Tata, James R.; Shen, Hong C.; Marley, Daria M.; Deng, Qiaolin; Frie, Jessica L.; Ding, Fa-Xianq
- PA Merck & Co., Inc., USA
- SO PCT Int. Appl., 125 pp.
  - CODEN: PIXXD2
- DT Patent LA English
- FAN.CNT 1

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OS MARPAT 144:488409

IT 688356-90-3P

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(drug candidate; preparation of N-acyl anthranilic acid and related compds. as niacin receptor agonists and their methods of treatment of dyslipidemias)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

## IT 887401-56-1P 887401-57-2P

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-acyl anthranilic acid and related compds as niacin receptor agonists and their methods of treatment of dyslipidemias)  $\[ \frac{1}{2} \]$ 

RN 887401-56-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (+)- (CA INDEX NAME)

Rotation (+).

RN 887401-57-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)-, (-)- (CA INDEX NAME)

Rotation (-).

IT 688356-71-0P 688356-95-8P 688357-06-4P 688357-08-6P 688357-09-7P 688357-10-0P

688357-11-1P 688357-12-2P 688357-13-3P

688357-14-4P 688357-15-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-acyl anthranilic acid and related compds. as nlacin receptor agonists and their methods of treatment of dyslipidemias)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

TT

AR The invention is related to a method of treating atherosclerosis, dyslipidemia and related conditions wherein a nicotinic acid receptor partial/agonist I, or one of its pharmaceutically acceptable salts or solvates, is administered to a human patient in combination with a DP receptor antagonist, e.g. II, in amts. that are effective for treatment in the absence of substantial flushing. The invention is also related to the preparation of tetrazole I and DP antagonists. Thus, I was prepared by reaction of cyclopentanone with diethylmalonate (no data for the intermediate), followed by cyclization with hydrazine hydrochloride, amidation of the ester with methanolic ammonia, dehydration of the amide, and cyclization of the nitrile with NaN3. An 11step synthesis was given for pyridoindolizine II (no data for the intermediates). II, and its derivs., having a binding affinity (Ki) for CRTH2 of about ≥ 0.5 µM, and a selectivity for the DP receptor over CRTH2 of at least about 10 fold, are useful to inhibit the flushing effect seen when tetrazole I or its pharmaceutically acceptable salts or solvates are administered alone.

AN 2006:212213 CAPLUS Full-text

DN 144:292761

TI Preparation of 3-(2H-tetrazol-5-yl)-1,4,5,6-tetrahydrocyclopentapyrazole as nicotinic agonist and pyridoindolizine derivatives as DP receptor antagonists, and their combination useful for treating atherosclerosis, dyslipidemias and related conditions

IN Waters, M. Gerard; Turner, Mervyn

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

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PΙ
    WO 2006026273
                         A2
                                20060309
                                           WO 2005-US30001
                                                                   20050824
     WO 2006026273
                         A3
                               20060908
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             SL. SM. SY. TJ. TM. TN. TR. TT. TZ. UA. UG. US. UZ. VC. VN. YU.
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                                            WO 2005-US30001
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    CASREACT 144:292761
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     Dichlorophenyl)sulfanyl]-1-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[3,4-
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     [[4-(trifluoromethyl)phenyl]thio]-6,7,8,9-tetrahydropyrido[3,2-b]indolizin-
     6-yl]acetic acid 688357-09-7P, [5-[(2-Chloro-4-
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     b]indolizin-6-yl]acetic acid 688357-10-0P 688357-11-1P
     688357-12-2F, [5-[(4-Methylphenyl)thio]-4-(methylsulfonyl)-6,7,8,9-
     tetrahydropyrido[3,2-b]indolizin-6-yl]acetic acid 688357-13-3P,
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     b]indolizin-6-yl]acetic acid 688357-14-4P 688357-15-5P
     , [5-[(4-Chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-
     tetrahydropyrido[4,3-b]indolizin-6-yl]acetic acid 794535-37-8P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (DP receptor antagonist; preparation of a nicotinic agonist and DP receptor
        antagonists, and their combination useful for treating atherosclerosis,
        dyslipidemias and related conditions)
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Pvrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenvl)thio]-6,7,8,9-

tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

688356-71-0 CAPLUS

RN

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-11-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

- RN 688357-12-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-13-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-15-5 CAPLUS
- CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

- RN 794535-37-8 CAPLUS
- CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

- L13 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
- AB A method of treating atherosclerosis is disclosed wherein nicotinic acid or another nicotinic acid receptor agonist is administered to the patient in combination with a DP receptor antagonist. The DP receptor antagonist is

administered to reduce, prevent or eliminate flushing that may otherwise occur.

- AN 2004:999670 CAPLUS Full-text
- DN 141:420447
- TI Method of treating atherosclerosis, dyslipidemias and related conditions
- IN Cheng, Kang; Waters, M. Gerard; Metters, Kathleen M.; O'Neill, Gary
- PA
- SO U.S. Pat. Appl. Publ., 33 pp.
- CODEN: USXXCO
- DT Patent
- LA English

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KR 2008003470	A	20080107	KR 2007-729888		20071221
			US 2003-470665P	P	20030515
			WO 2004-US14980	W	20040513
			KR 2005-721795	A3	20051115

IT	688356-71-0P	688356-89-0P	688356-90-3P
	688356-95-8P	688357-06-4P	688357-08-6P
	688357-09-7P	688357-10-0P	688357-11-1P
	688357-12-2P	688357-13-3P	688357-14-4P
	688357-15-5D	794535-27-85	

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of treating atherosclerosis, dyslipidemias and related conditions)

RN 688356-71-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)



RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 794535-37-8 CAPLUS

CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)-, (9R)- (CA INDEX NAME)

Absolute stereochemistry.

IT 688356-87-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(method of treating atherosclerosis, dyslipidemias and related conditions)

RN 688356-87-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, ethyl ester (CA INDEX NAME)

L13 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

- \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT \*
- AB Title compds. I [wherein G = O(CH2)1-2, S(CH2)1-2, (un)substituted C1-3alkyl; Ar = hetero/aryl optionally substituted with Rg; Q = CO2H, CONH2 and derivs., SO2NH2 and derivs., SO3H, PO3H2 and tetrazolyl; one of A, B, C, or D is N and the others are independently selected from CH and CRg; E = (CH2)a-X-(CH2)b, phenylene, cycloalkylidene, cycloalkylene, etc.; a, b = 0-1, X = abond, O, S, NH and derivs., etc.; F = (CH2)m and derivs., CH:CH and derivs.; m = 1-3; Rl = H, CN, OH and derivs., (un)substituted alkyl, etc.; R2 = H, alkyl optionally substituted with 1-6 halogens; RIR2 = oxo; or RIR2 = (un)substituted 3- or 4-membered ring, optionally containing 1 heteroatom; R3 = H, (un)substituted alkyl; Rg = halo, CN, CHO, CO2H and derivs., CONH2 and derivs., H2 and

derivs., NO2, alkoxy, OCONB2 and derivs., SO2-alkyl, (un)substituted alk/en/yl, etc.] were prepared as prostaglandin receptor, in particular PGD2, antagonists useful for the treatment of prostaglandin-mediated diseases such as allergic rhinitis, nasal congestion and asthma (no data). Six biol. assays are given (no data). Thus, reaction of II (preparation given) with a mixture of bis(3,4-dichlorophenyl)disulfide, SO2C12, 1,2-dichloroethane, followed by hydrolysis gave the pyridoindolizinyl acid III.

AN 2004:390250 CAPLUS Full-text

DN 140:406734

TI Preparation of pyridopyrrolizines and pyridoindolizines as prostaglandin receptor, in particular PGD2, antagonists

IN Leblanc, Yves; Dufresne, Claude; Rov, Patrick

PA Merck Frosst Canada & Co., Can.

SO PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DT Patent

LA English

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				US	2003-482626P	P	20030626
				WO	2003-CA1658	W	20031028

OS MARPAT 140:406734

ΙT

688356-87-8, Ethyl 2-[5-[(4-chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[3,2-b]indolizin-6-yl]acetate

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyridopyrrolizines and pyridoindolizines as prostaglandin D2 receptor antagonists)

RN 688356-87-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)-, ethyl ester (CA INDEX NAME)

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688356-71-0P, [5-[(4-Chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-
tetrahydropyrido[3,2-b]indolizin-6-yl]acetic acid 688356-89-0P,
[5-[(4-Chlorophenvl)thio]-4-(methylthio)-6,7,8,9-tetrahydropyrido[3,2-
b]indolizin-6-yl]acetic acid 688356-90-3P, [5-[(3,4-
Dichlorophenyl)thiol-4-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[3,2-
b]indolizin-6-yl]acetic acid 688356-95-8P, [5-[(4-
Bromophenvl)thio -4-(methylsulfonvl)-6.7.8.9-tetrahydropyrido[3.2-
b]indolizin-6-yl]acetic acid 688357-06-4P 688357-08-6P
688357-09-7P 688357-10-0P 688357-11-1P
688357-12-2P, [5-[(4-Methylphenyl)thio]-4-(methylsulfonyl)-6,7,8,9-
tetrahydropyrido[3,2-b]indolizin-6-yl]acetic acid 688357-13-3P,
[4-(Methylsulfonv1)-5-(phenylthio)-6,7,8,9-tetrahydropyrido[3,2-
b]indolizin-6-yl]acetic acid 688357-14-4P 688357-15-5P
, [5-[(4-Chlorophenyl)thio]-4-(methylsulfonyl)-6,7,8,9-
tetrahydropyrido[4,3-b]indolizin-6-yl]acetic acid 688357-29-1P
688357-30-4P 688357-31-5P 688357-32-6P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prostaglandin D2 receptor antagonist; preparation of pyridopyrrolizines and pyridoindolizines as prostaglandin D2 receptor antagonists)

RN 688356-71-0 CAPLUS CN Pyrido[3,2-b]indoli:

Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-89-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylthio)- (CA INDEX NAME)

RN 688356-90-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688356-95-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-06-4 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-08-6 CAPLUS

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

RN 688357-09-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-10-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-naphthalenylthio)- (CA INDEX NAME)

RN 688357-11-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-12-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-[(4methylphenyl)thio]-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-13-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(phenylthio)- (CA INDEX NAME)

RN 688357-14-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-15-5 CAPLUS

Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-(methylsulfony1)- (CA INDEX NAME)

RN 688357-29-1 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-1-(methylsulfony1)- (CA INDEX NAME)

RN 688357-30-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9tetrahydro-2-methyl-4-(methylsulfony1)- (CA INDEX NAME)

RN 688357-31-5 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-3-methyl-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-32-6 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-chlorophenyl)thio]-6,7,8,9tetrahydro-3-methyl-1-(methylsulfonyl)- (CA INDEX NAME)

- RN 688357-33-7 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-methyl-1-(methylsulfony1)- (CA INDEX NAME)

- RN 688357-34-8 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-fluorophenyl)thio]-6,7,8,9tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-35-9 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-36-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-37-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-38-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-39-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-40-6 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-fluorophenyl)thio]-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-41-7 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-42-8 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-43-9 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-bromopheny1)thio]-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 688357-44-0 CAPLUS
- CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

RN 688357-45-1 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(3,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

RN 688357-58-6 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-fluorophenyl)thio]-6,7,8,9tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-59-7 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chloropheny1)thio]-6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-60-0 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-61-1 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-bromophenyl)thio]-6,7,8,9tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-62-2 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-63-3 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-6,7,8,9-tetrahydro-4-(1-methylethyl)- (CA INDEX NAME)

RN 688357-64-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(1-methoxypropyl)- (CA INDEX NAME)

RN 688357-67-7 CAPLUS

CN Pyrido[4,3-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-4-(1-methoxypropyl)- (CA INDEX NAME)

RN 688357-68-8 CAPLUS

CN Pyrido[3,4-b]indolizine-9-acetic acid, 10-[(4-chloropheny1)thio]-6,7,8,9tetrahydro-1-(1-methoxypropy1)- (CA INDEX NAME)

RN 688357-70-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-chlorophenyl)thio]-4-(1,1-dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

RN 688357-71-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(3,4-dichlorophenyl)thio]-4-(1,1-dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

RN 688357-72-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(4-bromopheny1)thio]-4-(1,1dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

RN 688357-73-5 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 4-(1,1-dimethylethyl)-6,7,8,9tetrahydro-5-[[4-(trifluoromethyl)phenyl]thio]- (CA INDEX NAME)

- RN 688357-74-6 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2-chloro-4-fluorophenyl)thio]-4-(1,1-dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

- RN 688357-75-7 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 4-(1,1-dimethylethyl)-6,7,8,9tetrahydro-5-(2-naphthalenylthio)- (CA INDEX NAME)

- RN 688357-76-8 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,3-dichlorophenyl)thio]-4-(1,1-dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

RN 688357-77-9 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 4-(1,1-dimethylethyl)-6,7,8,9tetrahydro-5-[(4-methylphenyl)thio]- (CA INDEX NAME)

RN 688357-78-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 4-(1,1-dimethylethyl)-6,7,8,9tetrahydro-5-(phenylthio)- (CA INDEX NAME)

RN 688357-79-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,4-dichlorophenyl)thio]-4-(1,1-dimethylethyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)

RN

RN 688357-81-5 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1H-pyrrol-2-ylthio)- (CA INDEX NAME)

RN 688357-82-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1H-1,2,4-triazol-5-ylthio)- (CA INDEX NAME)

RN 688357-83-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1H-1,2,3-triazol-5-ylthio)- (CA INDEX NAME)

RN 688357-85-9 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-(1H-imidazol-5-ylthio)-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-86-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1H-pyrazol-4-ylthio)- (CA INDEX NAME)

RN 688357-87-1 CAPLUS

CN

Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1H-pyrazol-3-ylthio)- (CA INDEX NAME)

RN 688357-88-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-y1)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-89-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-(4-isothiazolylthio)-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-90-6 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(3-furanylthio)-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-91-7 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4 (methylsulfonyl)-5-(1,2,3-thiadiazol-4-ylthio)- (CA INDEX NAME)

RN 688357-92-8 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-

RN 688357-93-9 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-(4isoxazolylthio)-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-94-0 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(3-thienylthio)- (CA INDEX NAME)

RN 688357-95-1 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(4-oxazolylthio)- (CA INDEX NAME)

RN 688357-96-2 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(4-thiazolylthio)- (CA INDEX NAME)

RN 688357-97-3 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,5-dihydro-5-oxo-2furanyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-98-4 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-[(2,5-dihydro-5-oxo-3-furanyl)thio]-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688357-99-5 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(1,2,4-oxadiazol-5-ylthio)- (CA INDEX NAME)

- RN 688358-00-1 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(3-pyridinylthio)- (CA INDEX NAME)

- RN 688358-01-2 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-pyrazinylthio)- (CA INDEX NAME)

- RN 688358-02-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(5-pyrimidinylthio)- (CA INDEX NAME)

- RN 688358-03-4 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-5-(1H-indol-2-ylthio)-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688358-04-5 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(benzo[b]thien-2-ylthio)-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688358-05-6 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(2-benzofuranylthio)-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688358-06-7 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-[(4-oxo-4H-1-benzopyran-2-yl)thio]- (CA INDEX NAME)

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(2-quinolinylthio)- (CA INDEX NAME)

- RN 688358-08-9 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(1H-benzimidazol-2-ylthio)-6,7,8,9-tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688358-09-0 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(2-benzoxazolylthio)-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

- RN 688358-10-3 CAPLUS
- CN Pyrido[3,2-b]indolizine-6-acetic acid, 5-(2-benzothiazolylthio)-6,7,8,9tetrahydro-4-(methylsulfonyl)- (CA INDEX NAME)

RN 688358-12-5 CAPLUS

CN Pyrido[3,2-b]indolizine-6-acetic acid, 6,7,8,9-tetrahydro-4-(methylsulfonyl)-5-(thieno[2,3-b]pyridin-2-ylthio)- (CA INDEX NAME)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN GI

AB Title compds. I [wherein R1, R2, and R3 = independently H, halo, CN, CORa, CO2Ra, CONRARb, OCONRARb, SO0-2-(hetero)aryl, NRaSO0-2Rb, NRaRb, NRaCORb, NRaCO2Rb, NRaCONRaRb, SO0-2NRaRb, NO2, cycloalkenyl, or (un)substituted alkyl, alkenyl, alkoxy, heterocyclyl, (hetero)aryl(oxy), or SOO-2-alkyl; Ra and Rb = independently H or (un)substituted alkyl, alkenyl, alkynyl, heterocyclyl, or (hetero)arvl; or NRaRb = heterocyclyl; R4 = H, CN, (halo)alkyl, ORa, or SO0-2alkyl; R5 = H or (halo)alkyl; or CR4R5 = (un)substituted 3- or 4-membered (hetero)cycloalkyl; R6 = H or (un)substituted alkyl; Ar = (un)substituted (hetero)arvl; A = (un)substituted alkvl; O = CO2H, CONRARD, CONHSO2Rc, SO2NHRa, SO2NHRa, SO3H, PO3H2, or tetrazolyl; Rc = (un)substituted alkyl; Y1 = (un) substituted alkylidene optionally interrupted by O, S, NRa, CO, OCO, etc.; Y2 = (un)substituted methylene, ethylene, or ethenylene; and pharmaceutically acceptable salts and hydrates thereof) were prepared as non-steroidal D2 prostaglandin receptor antagonists (no data). For example, 4-[2-bromo-3-(4chlorobenzyl)-1H-1-indolyl]butanal (4-step preparation given) was coupled with (carbethoxymethylene)triphenylphosphorane to give the Et (E)-2-hexenoate. Cyclization using Bu4NCl, TEA, and Pd(AcO)2 in DMF afforded Et 2-[10-(4chlorobenzyl)-6,7,8,9-tetrahydropyrido[1,2- a]indol-9-yliden]acetate. Reduction with Pd/C (5%, weight/weight) followed by saponification with LiOH in MeOH provided II. I are useful for the treatment of prostaglandin-mediated diseases such as allergic rhinitis, nasal congestion, and asthma (no data). 2002:906233 CAPLUS Full-text AN

- DN 138:4518
- TI Preparation of dihydropyrrolo[1,2-a]indole and tetrahydropyrido[1,2-a]indole derivatives as prostaglandin D2 receptor antagonists for treatment of allergic rhinitis, nasal conqestion, and asthma
- IN Wang, Zhaoyin; Dufresne, Claude; Guay, Daniel; Leblanc, Yves PA Merck Frosst Canada & Co., Can.; Beaulieu, Christian
- PA Merck Frosst Canada & Co., Can.; Beaulieu, Christian SO PCT Int. Appl., 225 pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

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## OS MARPAT 138:4518

IT

- 476620-31-2P, [10-[(4-Chlorophenyl)thio]-3-fluoro-1-isopropyl-
- 6,7,8,9-tetrahydropyrido[1,2-a]indol-9-yl]acetic acid 476620-37-8P, [10-{(4-Chlorophenyl)thio]-3-fluoro-1-(methylsulfonyl)-6,7,8,9-tetrahydropyrido[1,2-a]indol-9-yl]acetic acid 476620-75-4P 476620-61-2P
- RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prostaglandin D2 receptor antagonist; preparation of pyrroloindole and

pyridoindole prostaglandin D2 receptor antagonists by cyclization of (indolyl)alkanoates and (indolyl)alkanoates)

- RN 476620-31-2 CAPLUS
- CN Pyrido(1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 476620-37-8 CAPLUS
- CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-3-fluoro-6,7,8,9-tetrahydro-1-(methylsulfonyl)- (CA INDEX NAME)

- RN 476620-75-4 CAPLUS
- CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(3-bromo-4-chlorophenyl)thio]-3fluoro-6,7,8,9-tetrahydro-1-(1-methylethyl)- (CA INDEX NAME)

- RN 476620-81-2 CAPLUS
- CN Pyrido[1,2-a]indole-9-acetic acid, 10-[(4-chlorophenyl)thio]-6,7,8,9-tetrahydro-1-(methylsulfonyl)-3-(phenylmethoxy)- (CA INDEX NAME)